

Gene name: O1-180

cDNA sequence: 1276 bp

“AAGGCGGGCGAGGCGCGGGACGCACCCATGTTCCCGGGCGAG
CACGTTCCACCCCTGCCCGCATCCTTATCCGCAGGCCACCAAAGCCGGGGATG
GCTGGAGGTTCGGAGCCAGGGGCTGCCGACCCGCGCCCCCTCCTTCTCTCCC
GGCTACAGACAGCTCATGGCCGCGGAGTACGTGACAGCCACCAGCGGGCAC
AGCTCATGGCCCTGCTGTGCGGGATGGGTCCCCGGTCGGTCAGCAGCCGTGA
CGCTGCGGTGCAGGTGAACCCGCGCCGACGCCTCGGTGCAGTGTCTACTC
GGGCGCCGCACGCTGCAGCCTGCAGGGTGCCGAGCCAGCCCCGACGCCCCGAT
CGGGTTCCTGTCAACCCCGTGGCCACGCCGGCGCCGGGAGATCCCCGCGATC
CTGGCAGACCGTAGCCCCGTTCTCGTCCGTGACCTTCTGTGGCCTCTCCTCCTC
ACTGGAGGTTCGGGGAGGCAGGCAGACACCCACGAAGGGAGAGGGGAGCCC
GGCATCCTCGGGGACCCGGGAACCGGAGCCGAGAGAGGTGGCCGCGAGGAA
AGCGGTCCCCCAGCCGCGAAGCGAGGAGGGCGATGTTCAAGGTGCAGGGCA
GGCCGGGTGGGAGCAGCAGCCACCACCGGAGGACCGGAACAGTGTGGCGGC
GATGCAGTCTGAGCCTGGGAGCGAGGAGCCATGTCCTGCCGCAGAGATGGCT
CAGGACCCCGGTGATTCCGATGCCCTCGAGACCAGGCCTCCCCGCAAAGCAC
GGAGCAGGACAAGGAGCGCCTGCGTTTCCAGTTCTTAGAGCAGAAGTACGGCT
ACTATCACTGCAAGGACTGCAAAATCCGGTGGGAGAGCGCCTATGTGTGGTGT
GTGCAGGGCACCAGTAAGGTGTTACTTCAAACAGTTCTGCCGAGTGTGTGAGAA
ATCCTACAACCCTTACAGAGTGGAGGACATCACCTGTCAAAGTTGTAAAAGAAC
TAGATGTGCCTGCCCAGTCAGATTTGCGCCACGTGGACCCTAAACGCCCCCATC
GGCAAGACTTGTGTGGGAGATGCAAGGACAAACGCCTGTCCTGCGACAGCAC
CTTCAGCTTCAAATACATCATTTAGTGAGAGTCGAAAACGTTTCTGCTAGATGG
GGCTAATGGAATGGACAAGTGAGCTTTCTCCCCTCTTCACCTCTTCCCTTTCCAA
ATTCTTCATGACAGACAGTGTACTTGGATATAAAGCCTGTGAATAAAAGGTAT
TGCAAAACAAAAAAAAAAAAAAAAAAAA”

Figure 1

Amino Acid sequence: 361aa

"MFPASTFHPCPHYPQATKAGDGWRFGARGCRPAPPSFLPGYRQLMAAEYVDS
HORAQLMALLSRMGPRSVSSRDAAVQVNPRRDASVQCSLGRRTLQPAGCRASPDA
RSGSCQPRGHAGAGRSPRSWQTVAPFSSVTFGLSSSLEVAGGRQTPTKGEGLSPA
SSGTREPEPREVAARKAVPQPRSEEGDVQAAGQAGWEQQPPPEDRNSVAAMQSEP
GSEEPCPAAEMAQDPGDSAPRDQASPOSTEQDKERLRFQFLEQKYGYHCKDCK
IRWESAYVWCVQGTSKVYFKQFCRVCEKSYNPHYRVEDITCQSKRTRCACPVRF
HVDPKRPHRQDLGGRCKDKRLSCDSTFSFKYII"

Figure 2

01-184 cDNA sequence: 1817bp

GTCACAGCTTTCCCCTGCCCCGAATATGGTGATCTGTCTCCATTGTCCAGATCA
GGATGATTCTTTAGAAGAAGTCACAGAGGAATGCTATTCCCCACCCACCCTC
CAGAACCTGGCAATTCAGAGTCTACTGAGGGATGAGGCCTTGGCCATTTCTG
CTCTCACGGACCTGCCCCAGAGTCTGTTCCCAGTAATTTTTGAGGAGGCCTTC
ACTGATGGATATATAGGGATCTTGAAGGCCATGATACCTGTGTGGCCCTTCCC
ATACCTTTCTTTAGGAAAGCAGATAAATAATTGCAACCTGGAGACTTTGAAG
GCTATGCTTGAGGGACTAGATATACTGCTTGCACAAAAGGTTCAAACAGTA
GGTGCAAACTCAGAGTAATTAATTGGAGAGAAGATGACTTGAAGATATGGGC
TGGATCCCATGAAGGTGAAGGCTTACCAGATTTTCAAGGACAGAGAAGCAGCCA
ATTGAGAACAGTGCTGGCTGTGAGGTGAAGAAAGAATTGAAGGTGACGACT
GAAGTCCTTCGCATGAAGGGCAGACTTGATGAATCTACCACATACTTGTTC
AGTGGGCCCAGCAGAGAAAAGATTCTATTCATCTATTCTGTAGAAAGCTACT
AATTGAAGGCTTAACCAAAGCCTCAGTGATAGAAATCTTCAAACTGTACAC
GCAGACTGTATACAGGAGCTTATCCTAAGATGTATCTGCATAGAAGAGTTGG
CTTTTCTTAATCCCTACCTGAAACTGATGAAAAGTCTTTTCACTCACACTA
GATCACATCATAGGTACCTTCAGTTTGGGTGATTCTGAAAAGCTTGATGAGG
AGACAATATTCAGCTTGATTTCTCAACTTCCCACACTCCACTGTCTCCAGAAA
CTCTATGTAAATGATGTCCCTTTTATAAAAGGCCAACCTGAAAGAATACCTCAG
GTGCCTGAAAAAGCCCTTGGAGACACTTTGCATCAGTAACTGTGACCTCTCAC
AGTCAGACTTGGATTGCCTGCCCTATTGCCTGAATATTTGTGAACTCAAACAT
CTGCATATTAGTGATATATATTTATGTGATTTACTCCTTGAGCCTCTTGTTTT
CTCCTTGAGAGAGTTGGAGATACCCTGAAAACCCTGGAATTGGATTGATGTT
GTATAGTGGACTTTTCAGTTCAGTGCCCTTGCTGCCTGCCCTAAGCCAATGTTCT
CACCTCAGAGAGGTCACTTTCTATGATAATGATGTTTCTCTGCCTTTCTTGAA
AACAACTTCTACACCACACAGCCCTGCTGAGTCAGCTGATCTATGAGTGTTAC
CCTGCCCCTCTAGAGTGCTATGATGACAGTGGTGTAACTAACACACAGATT
AGAAAGTTTTTGTCTGAGCTTCTGGATATACTGAGAGCCAAAAGACAGCTC
CATAGTGTCTCCTTTCAAACAACCAAATGCTCTAAATGTGGTGGGTGCTACAT
TTATGATCGGCATACCCAATGTTGCCGTTTTGTGGAAGTACTATAAGCTTGAT
TGTGAAACTGAGAAATAGAACTTAGTATTGGGGACTGATGAAATCCTAAGT
GAATGTCCACTGCTAAATGGAGCATGAAAATGTCAATCACCTAAAAGTCTGA
GATACACAGGAAAGTCAATAACTTCTCTGAGCTGGTGAATGGATGTTGCAT
CTGTAGAAAGTATCAAGCACTTGTAGTTTGAATGTGTTACAATAGAAGCACC
ATTTTATGAGACTGGCCCAATCTGTTGACTGCATACAATAAATCTGTTGACTT
ATTAAATTTTTAAAAAAAAAAAAAAAAAAAAA

Figure 3

O1-184 amino acid sequence: 426 amino acids

MVICLHCPDQDDSL EEVTEECYSPPTLQNLAIQSLLRDEALAI SALTDL PQSLFP
VIFEEAFTDGYIGILKAMIPVWPFPYLSLGKQINNONLET LKAMLEGLDILLAQKV
QTSRCKLRVINWREDDLKIWAGSHEGEGLPDFRTEKQPIENSAGCEVKKELKV
TTEVLRMKGRLDESTTYLLQWAQQRKDSIHLFCRKLLIEGLTKASVIEIFKTVHA
DCIQELILRCICIEELAF LNPYLKLMKSLFTLTLDHIIGTFSLGDSEKLDEETIFSLIS
QLPTLHCLQKLYVNDVPFIKGNLKEYLRCLKKPLETLCISNCDLSQSDLDCLPYC
LNICELKHLHISDIYLC D L L L E P L G F L L E R V G D T L K T L E L D S C C I V D F Q F S A L L P A L
SQCSHLREVT FYDNDVSLPFLKTTSTPHSPAESADL

Figure 4

Gene name: O1-236

cDNA sequence: 1019bp

“GCCATATTGAGGACCTGCAGTAGAGGTGGAACCCATGACTGGCAGCGCAAAC
ACAGTGATAACAGCTGAGCTCCAAGCAAGGACCCAGGACCTTGCCTCACCACA
GACATAATCTTTCCCCACAACACCTCCACCAAGCCGCCCTGTAAATCGACATGA
GTCGCCACAGCACCAGCAGCGTGACCGAAACACAGCAAAAAACATGCTCTGG
GGTAGTGAACCTCAATCAGGAAAAGCAGACTTGCACCTTTAGAGGCCAAGGCCA
GAAGAAGGACAGCTGTAAACTCTTGCTCAGCACGATCTGCCTGGGGGAGAAAG
CCAAAGAGGAGGTGAACCGTGTGGAAGTCCTCTCCAGGAAGGCAGAAAACC
ACCAATCACTATTGCTACGCTGAAGGCATCAGTCCTGCCCATGGTCACTGTGTC
AGGTATAGAGCTTTCTCCTCCAGTAACTTTTCGGCTCAGGACTGGCTCAGGACC
TGTGTTCTCCTCAGTGGCCTGGAATGTTATGAGACTTCGGACCTGACCTGGGAAG
ATGACGAGGAAGAGGAGGAAGAGGAGGAAGAGGATGAAGATGAGGATG
CAGATATATCGCTAGAGGAGATACCTGTCAAACAAGTCAAAAGGGTGGCTCCC
CAGAAGCAGATGAGCATAGCAAAGAAAAAGAAGGTGGAAGAAAGAGGATG
AAACAGTAGTGAGGCCCCAGCCCTCAGGACAAGAGTCCCTGGAAGAAGGAGAA
ATCTACACCCAGAGCAAAGAAGCCAGTGACCAAGAAATGACCTCATCTTAGCAT
CTTCTGCGTCCAAGGCAGGATGTCCAGCAGCTGTGTTTTGGTGCAGGTGTCCA
GCCCCACCAACCTAGTCTGAATGTAATAAGGTGGTGTGGCTGTAACCCTGTAAC
CCAGCCCTCCAGTTTCCGGAGGTTTTTGGTGAAGAGCCCCCAGCAAGTTCGCC
TAGGGCCACAATAAAATTTGCATGATCAGGAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAA”

Figure 5

Amino Acid sequence: 207aa

“MSRHSTSSVTETTAKNMLWGSELNQEKQTCTFRGQGEKKDSCKLLLSTICLGEK
AKEEVNRVEVLSQEGRKPPITIALTKASVLPMTVSGIELSPVTFRLRTGSGPVFLS
GLECYETSDLTWEDDEEEEEEEEEDEDEDADISLEEIPVKQVKRVAPQKQMSIAKK
KKVEKEEDET VVRPS PQDKSPWKKEKSTPRAKKPVTKK”

Figure 6

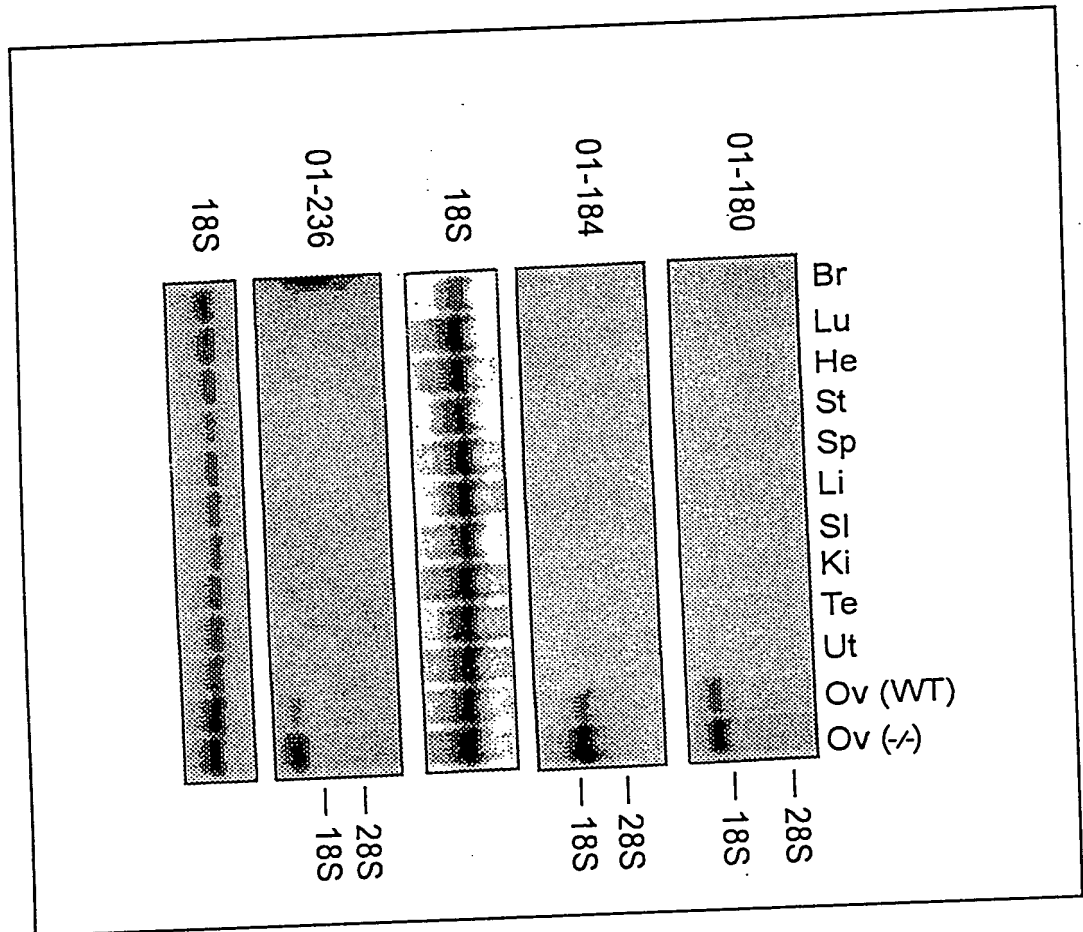


Figure 7

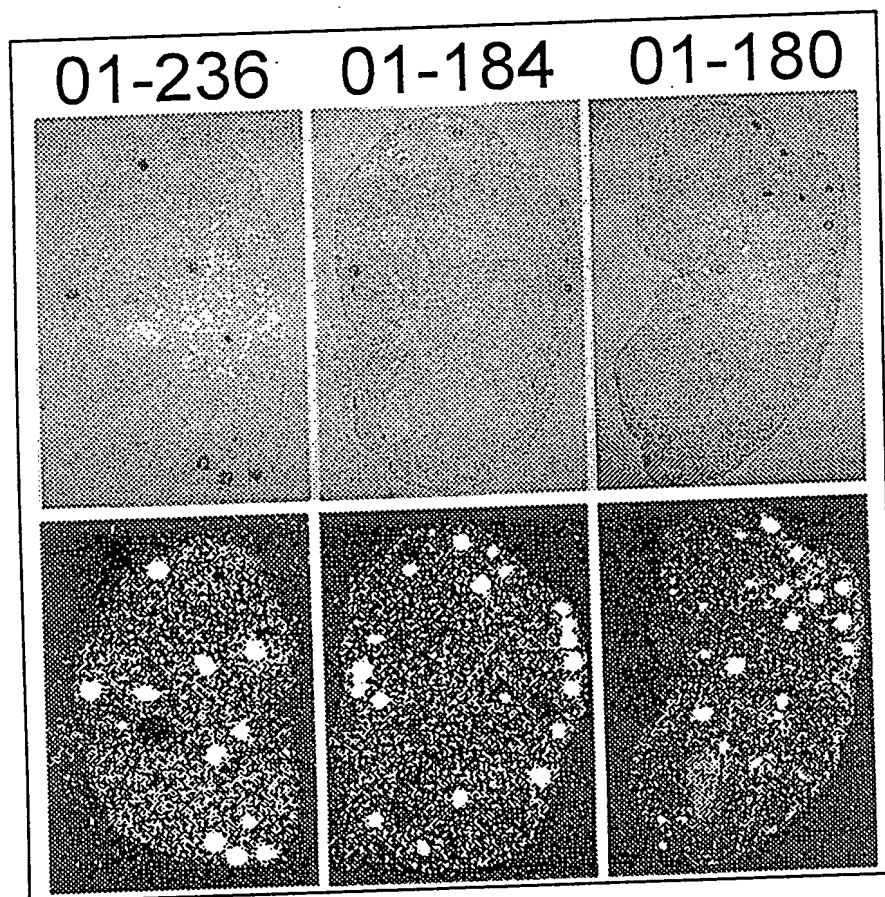


Figure 8

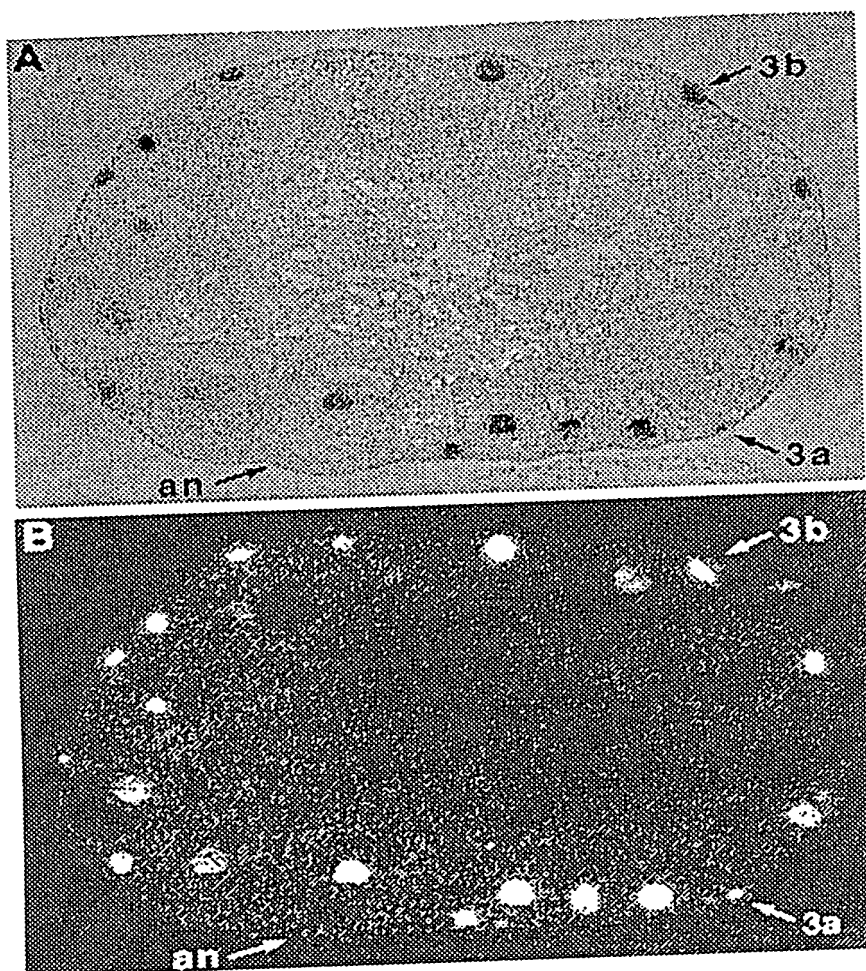


Figure 9

10/29

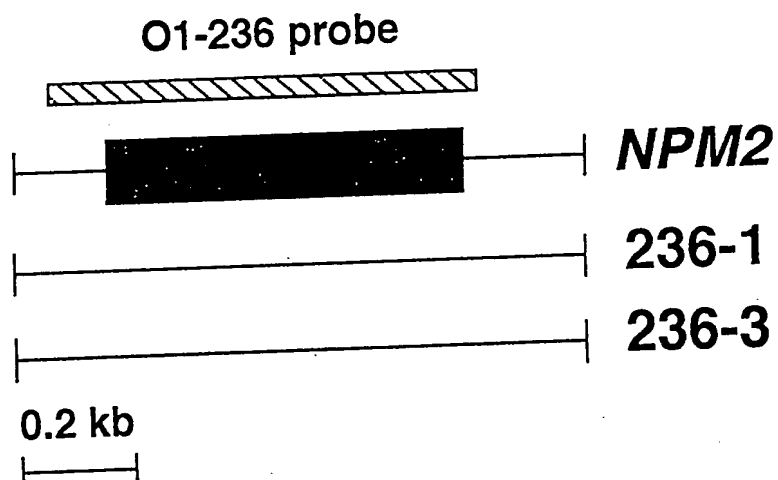


Figure 10

Npm2 MSRHSTSSVTETTAK--NMLWGSELN-QEKQTCTFRGQG-EKKDSCKLLL
 Xnpm2 MA--STVSNTSKLEKPVSLIWGCELNEQDK-TFEFKVEDDEEKCEHQLAL

PKC
 47 STICLGEKAKEEVNRVEVLSQE-GRKPPITIA~~TL~~KASVLPMTVSGIELS
 48 RTVCLGDKAKDEFNIVEIVTQEEGAEKSVPIA~~TL~~KPSILPMATMVGIELT

PKC CK2
 96 PPVTFRLRTGSGPVFLSGLECYETSDLT~~TWEDDEEEEEEEEEDEDEDAD~~
 98 PPVTFRLKAGSGPLYISGQHVAMEEDYSWA~~EEDEGEAEGEEEEEEEED~~

CK2
 146 SLEEIPVKQV~~KR~~VAPQKQMSIA~~KKKK~~VEKEEDET~~VVR~~PS~~QDK~~SPWKKEK
 147 --QESPPKAV~~KR~~PAATKKAGQA~~KKKK~~LDKE-DE-----~~SSEED~~SPTKKGK

196 STPRAKKPVTKK 207
 189 GAGRGRKPAACK 200

Figure 11

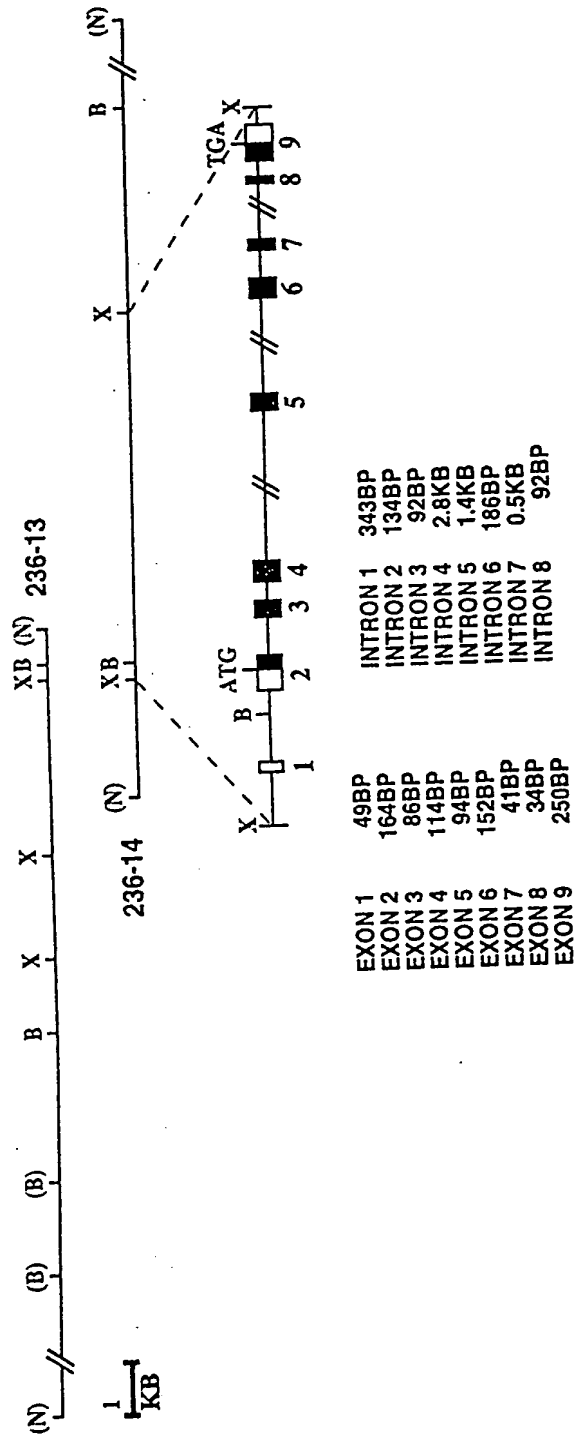


Figure 12

Mouse *Npm2* Gene Sequences

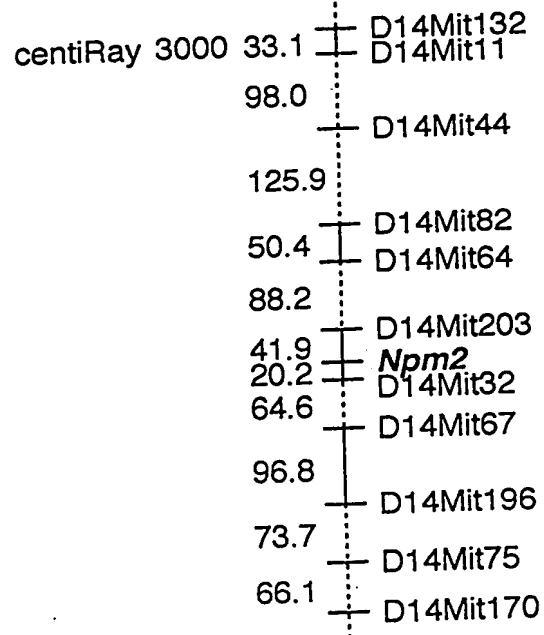
acagcagaggtgatgctcagaaatcaagttttaacagagggccaggtg
 cttctagagtaggaggggattgcacacctccccacccctcctctttc
 ccaggcttcttaacagcctgctgtgggaagctgaccttagatggagc
 cctgaaGCCATATTGAGGACCTGCAGTAGAGGTGGAACCCATGACTGG
 CAGCGCAgtaagcttgagcagg... intron 1= 343bp
 ...ctttgcattactcagAACACAGTGATAACAGCTGAGCTCCAAGCA
 AGGACCCAGGACCTTGCCTCACCACAGACATAATCTTTCCCCACAACA
 CCTCCACCAAGCCGCCCTGTAAATCGAC ATG AGT CGC CAC AGC
 M S R H S
 1
 ACC AGC AGC GTG ACC GAA ACC ACA GCA AAA AAC ATG
 T S S V T E T T A K N M
 6
 CTC TGG Ggtaagggtctaaggct... intron 2 = 134bp
 L W
 18
 ...gtcttcgctgtgcagGT AGT GAA CTC AAT CAG GAA AAG
 G S E L N Q E K
 20
 CAG ACT TGC ACC TTT AGA GGC CAA TGC GAG AAG AAG
 Q T C T F R G Q C E K K
 28
 GAC AGC TGT AAA CTC TTG CTC AGC ACGgtgggtgtctccc
 D S C K L L L S T
 40
 aa... intron 3 = 92bp ...catcacctttctcagATC
 I
 49
 TGC CTG GGG GAG AAA GCC AAA GAG GAG GTG AAC CGT
 C L G E K A K E E V N R
 50
 GTG GAA GTC CTC TCC CAG GAA GGC AGA AAA CCA CCA
 V E V L S Q E G R K P P
 62
 ATC ACT ATT GCT ACG CTG AAG GCA TCA GTC CTG CCC
 I T I A T L K A S V L P
 74
 ATGgtgagtcttctctcc... intron 4 = 2.8kb ...agaa
 M
 86
 gggggacacagGTC ACT GTG TCA GGT ATA GAG CTT TCT
 V T V S G I E L S
 87
 CCT CCA GTA ACT TTT CGG CTC AGG ACT GGC TCA GGA
 P P V T F R L R T G S G
 96

Figure 13A

108 CCT GTG TTC CTC AGT GGC CTG GAA TGT TAT Ggtaagtt
 P V F L S G L E C Y
 gtagccta... intron 5 = 1.35kb ...ggctacccattcc
 118 agAG ACT TCG GAC CTG ACC TGG GAA GAT GAC GAG GAA
 E T S D L T W E D D E E
 130 GAG GAG GAA GAG GAG GAG GAA GAG GAT GAA GAT GAG
 E E E E E E E E D E D E
 142 GAT GCA GAT ATA TCG CTA GAG GAG ATA CCT GTC AAA
 D A D I S L E E I P V K
 154 CAA GTC AAA AGG GTG GCT CCC CAG AAG CAG ATG AGC
 Q V K R V A P Q K Q M S
 166 ATA GCA AAGgtgggggaaaagaa... intron 6 = 186bp
 I A K
 169 ...tggttttgttccagAAA AAG AAG GTG GAA AAA GAA
 K K K V E K E
 176 GAG GAT GAA ACA GTA GTG AGgtaattcatgcagtt...
 E D E T V V R
 183 intron 7 = 0.5kb ... ctattccctttccagG CCC AGC
 P S
 185 CCT CAG GAC AAG AGT CCC TGG AAG AAG gtgagcaataag
 P Q D K S P W K K
 194 aag... intron 8 = 92bp ...ctcttatctgcacagGAG
 E
 195 AAA TCT ACA CCC AGA GCA AAG AAG CCA GTG ACC AAG
 K S T P R A K K P V T K
 207 AAA TGA CCTCATCTTAGCATCTTCTGCGTCCAAGGCAGGATGTCCA
 K *
 GCAGCTGTGTTCTGGTGCAGGTGTCCAGCCCCACCACCCTAGTCTGAA
 TGTAATAAGGTGGTGTGGCTGTAACCCTGTAACCCAGCCCTCCAGTTT
 CCGGAGGTTTTTGGTGAAGAGCCCCCAGCAAGTTCGCCTAGGGCCACA
 ATAAAATTTGCATGATCAGGacctccctctgcctccccctccctgat
 gggctcctcgctgctgcgatagctcatgtgccagcagagggaacc
 acgagcaagaaccagccccatgt

Figure 13B

T31 RH Chr 14



Haplotypes for T31 Chr 14 near Npm2

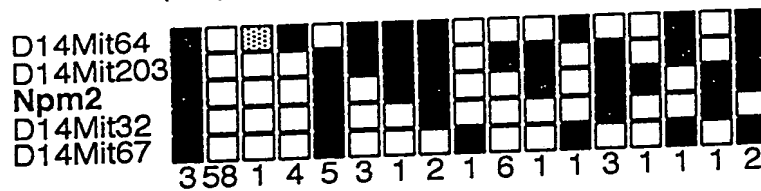


Figure 14

hNPM2	M	N	L	S	A	S	S	T	E	K	A	V	T	V	L	W	G	C	E	L	S	Q	E	R	R	T	W	T	F	R	P	Q	L	E	G	K	Q			
mNpm2	M	S	R	H	S	T	S	S	V	T	E	T	A	K	N	M	L	W	G	S	E	L	N	Q	E	K	Q	T	C	T	F	R	G	Q	E	K	D			
xNpm2	M	A	S	T	V	S	N	T	S	K	L	E	K	P	V	S	L	I	W	G	C	E	L	N	E	Q	D	K	T	F	E	F	K	V	E	-	D	D	E	E

hNPM2	S	C	-	-	R	L	L	L	H	T	I	C	L	G	E	K	A	K	E	E	M	H	R	V	E	I	L	P	P	A	N	Q	E	D	K	K	M	Q	P	V
mNpm2	S	C	-	-	K	L	L	L	S	T	I	C	L	G	E	K	A	K	E	E	V	N	R	V	E	V	L	S	-	-	Q	E	G	R	K	-	P	P	I	
xNpm2	K	C	E	H	Q	L	A	L	R	T	V	C	L	G	D	K	A	K	D	E	F	N	I	V	E	I	V	T	Q	E	E	G	A	E	K	S	V	P	-	-

hNPM2	T	I	A	S	L	Q	A	S	V	L	P	M	V	S	M	V	G	V	Q	L	S	P	P	V	T	F	Q	L	R	A	G	S	G	P	V	F	L	S	G	Q
mNpm2	T	I	A	T	L	K	A	S	V	L	P	M	V	T	V	S	G	I	E	L	S	P	P	V	T	F	R	L	R	T	G	S	G	P	V	F	L	S	G	L
xNpm2	-	I	A	T	L	K	P	S	I	L	P	M	A	T	M	V	G	I	E	L	T	P	P	V	T	F	R	L	K	A	G	S	G	P	L	Y	I	S	G	Q

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
mNpm2	E	C	Y	E	T	S	D	L	T	W	E	E	D	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-
xNpm2	H	V	A	M	E	E	D	Y	S	W	A	E	E	E	D	E	G	E	A	E	G	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-

hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	-	-

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																				
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																				
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K																			

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
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hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	-	

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																				
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																				
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K																			

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
mNpm2	E	C	Y	E	T	S	D	L	T	W	E	E	D	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	
xNpm2	H	V	A	M	E	E	D	Y	S	W	A	E	E	E	D	E	G	E	A	E	G	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	

hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																			
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																			
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K																		

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
mNpm2	E	C	Y	E	T	S	D	L	T	W	E	E	D	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	
xNpm2	H	V	A	M	E	E	D	Y	S	W	A	E	E	E	D	E	G	E	A	E	G	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	

hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																			
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																			
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K																		

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
mNpm2	E	C	Y	E	T	S	D	L	T	W	E	E	D	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	
xNpm2	H	V	A	M	E	E	D	Y	S	W	A	E	E	E	D	E	G	E	A	E	G	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	

hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																			
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																			
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K																		

hNPM2	E	R	Y	E	A	S	D	L	T	W	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	Q
mNpm2	E	C	Y	E	T	S	D	L	T	W	E	E	D	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	
xNpm2	H	V	A	M	E	E	D	Y	S	W	A	E	E	E	D	E	G	E	A	E	G	E	E	E	E	E	E	E	E	E	E	E	E	E	E	-	

hNPM2	S	P	V	K	Q	V	K	R	L	V	P	Q	K	Q	A	S	V	A	K	K	K	K	L	E	K	E	E	E	E	E	E	E	E	E	E	E	E	E
mNpm2	I	P	V	K	Q	V	K	R	V	A	P	Q	K	Q	M	S	I	A	K	K	K	K	V	E	K	E	E	E	E	E	E	E	E	E	E	E	E	
xNpm2	-	P	P	K	A	V	K	R	P	A	A	T	K	K	A	G	Q	A	K	K	K	K	L	D	K	E	D	E	-	-	-	-	-	-	-	-	-	

hNPM2	P	V	K	K	A	K	A	T	A	R	A	K	K	P	G	F	K	K																			
mNpm2	P	W	K	K	E	K	S	T	P	R	A	K	K	P	V	T	K	K																			
xNpm2	P	T	K	K	G	K	G	A	G	R	G	R	K	P	P	A	A	K	K</																		

FIGURE 15

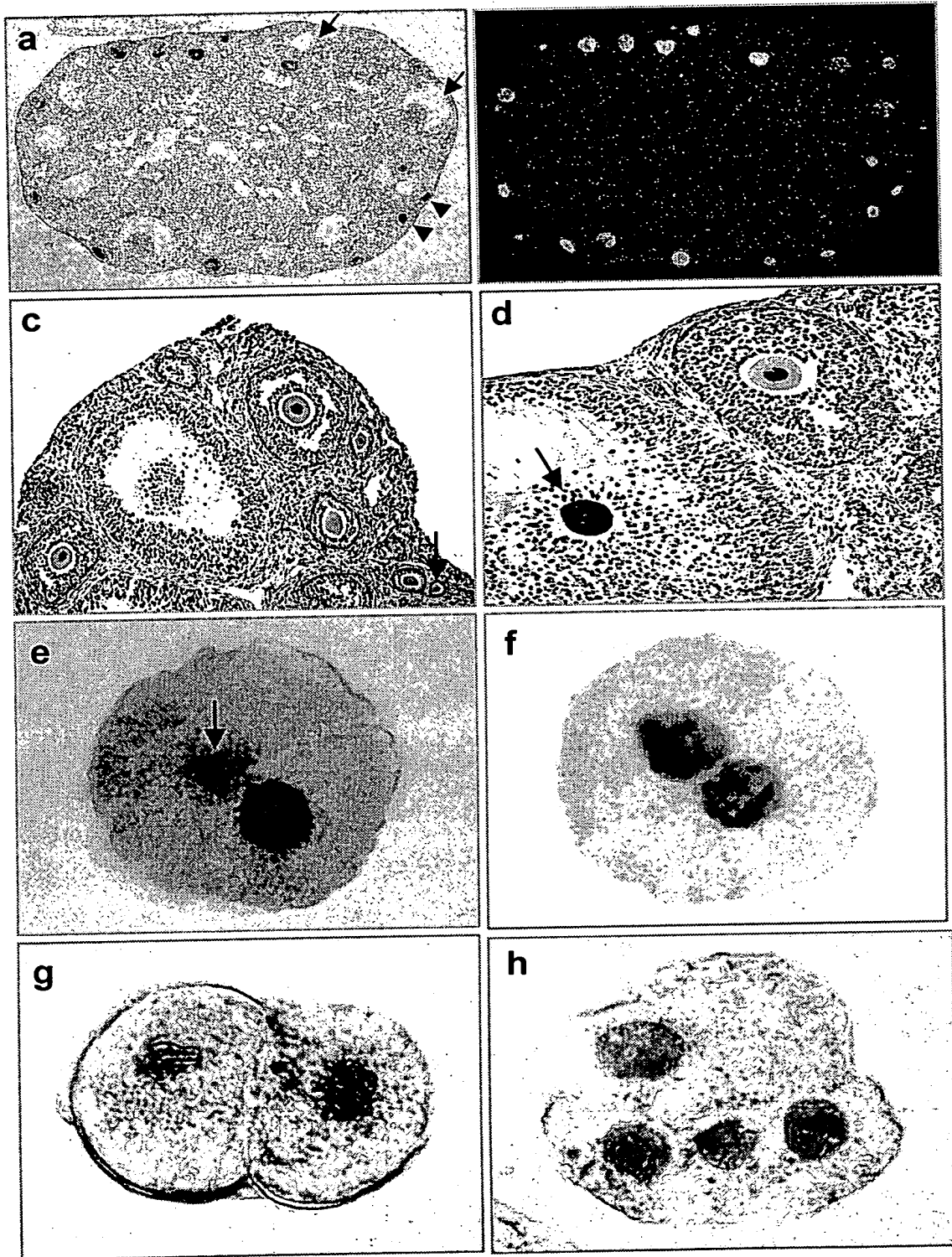


FIGURE 16

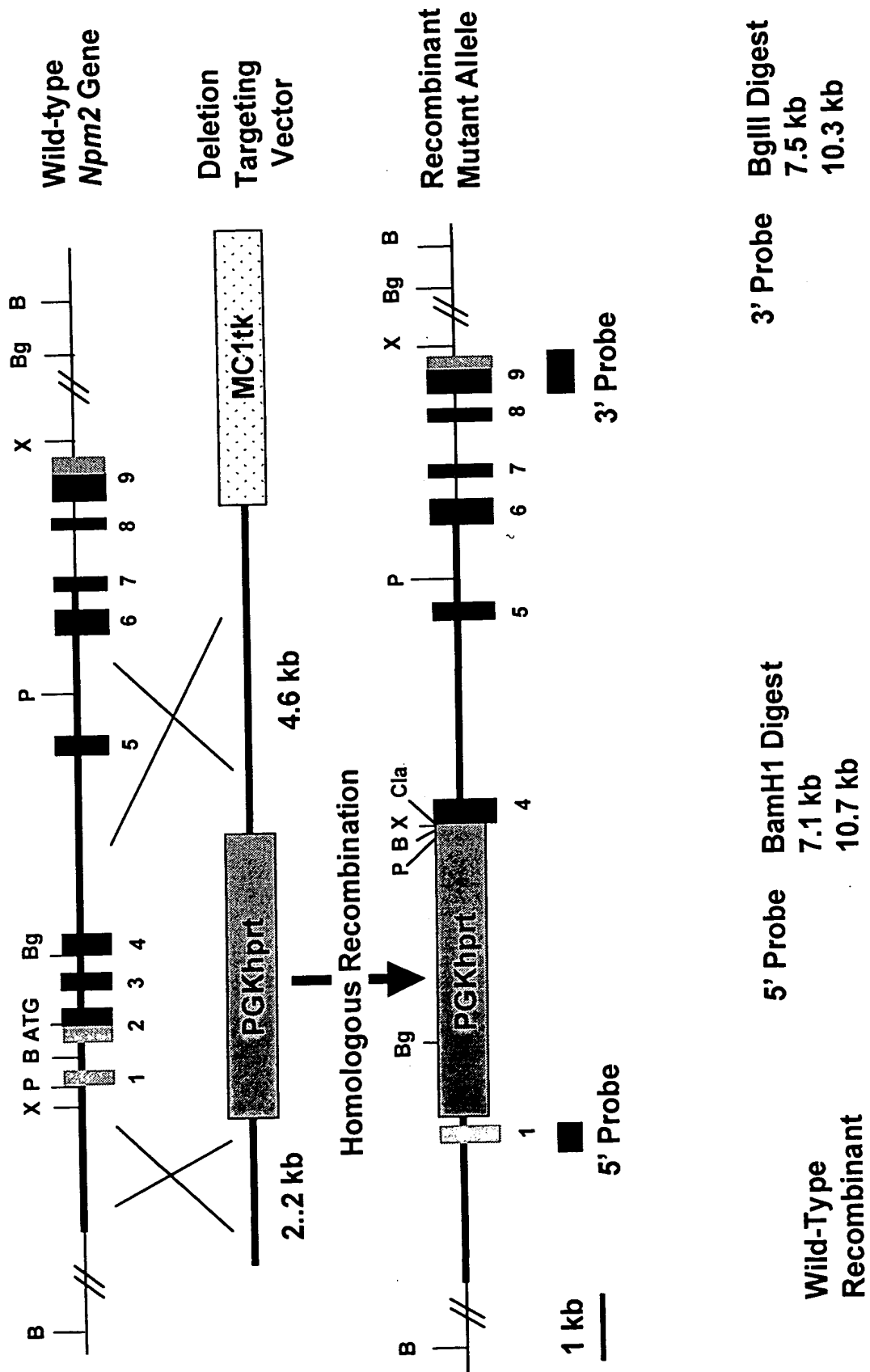


FIGURE 17a

10/23/03

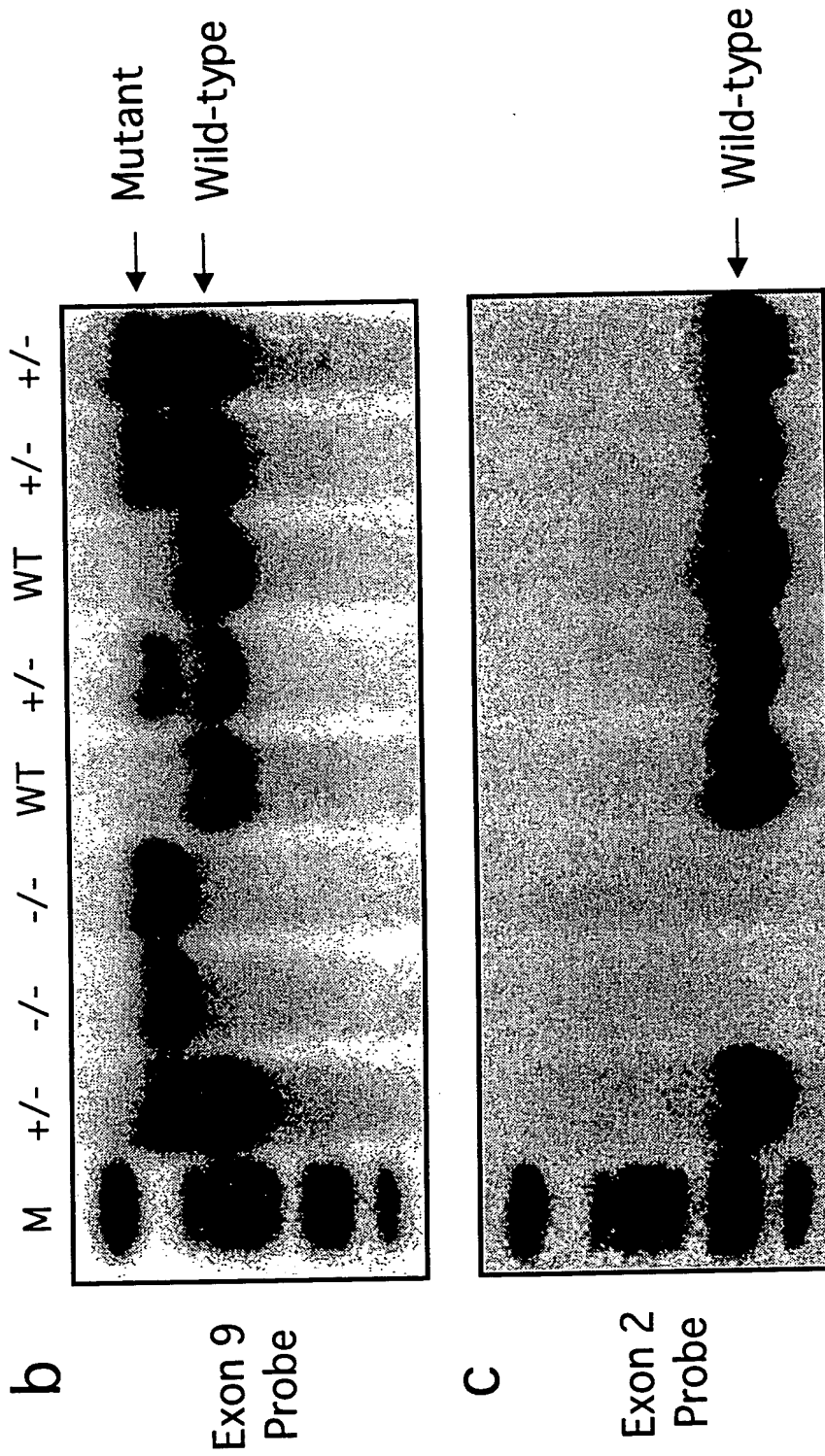


Figure 17b - Figure 17c

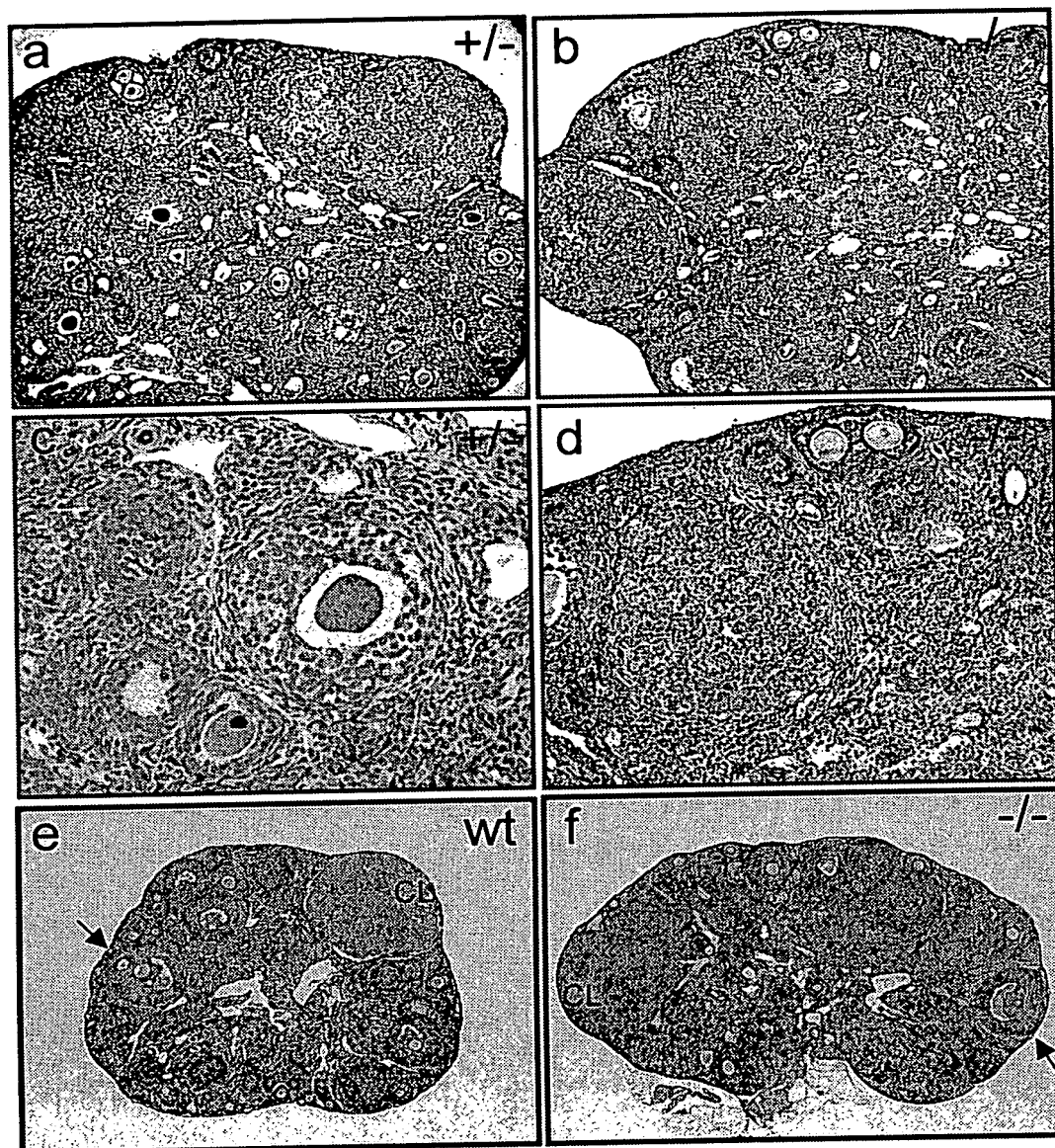


Figure 18

T0240-19344360

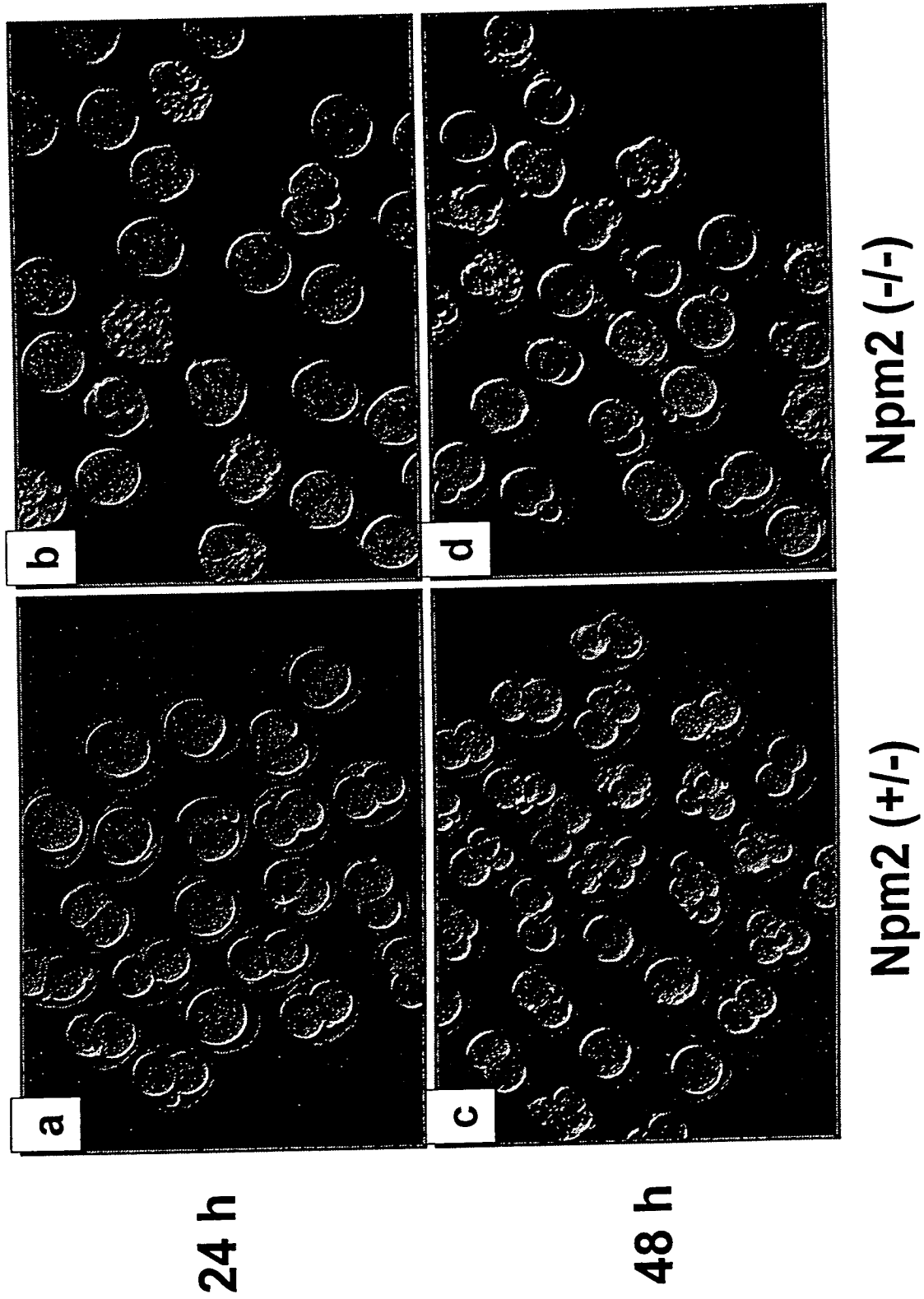


Figure 19a - 19d

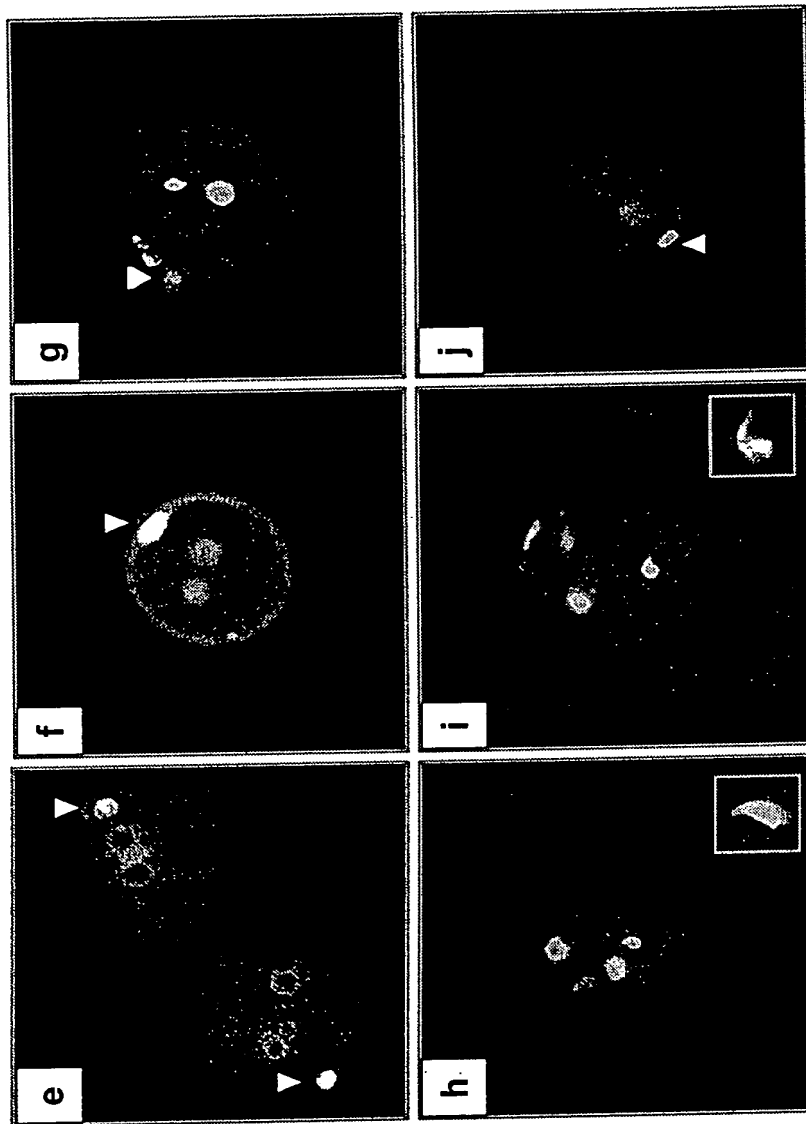


Figure 19e - 19j

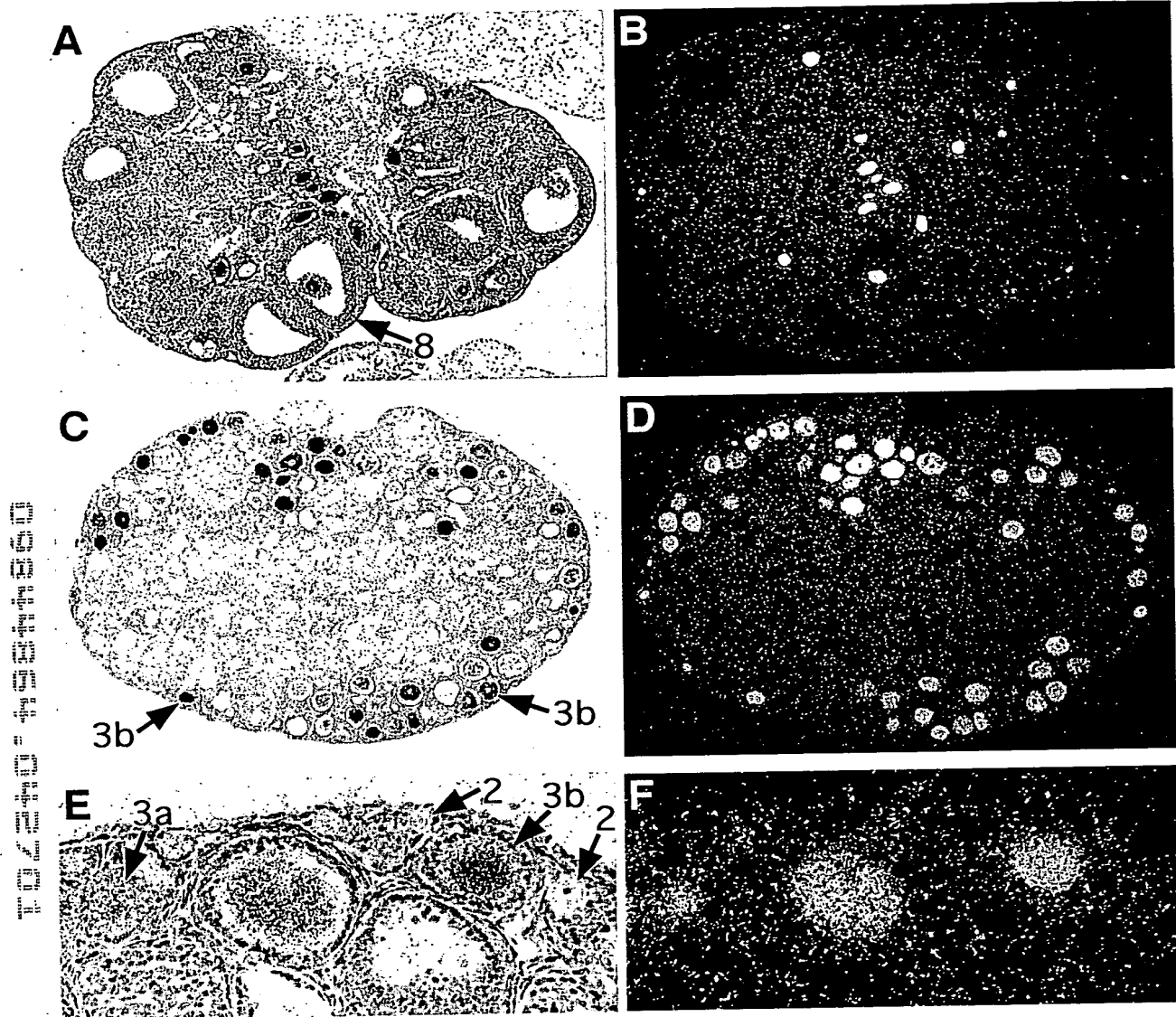


Figure 20

Oo1ps:

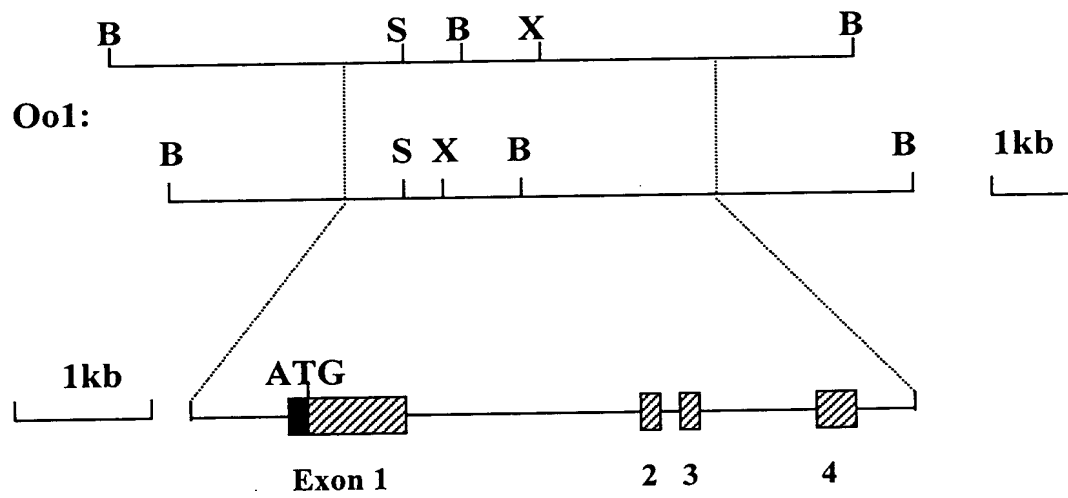


Figure 21

Oo1	gene	GGCGGGGAGGCGGGGACGCAACCATGTTCCCGGCGAGCAGCTTCCACCCCTGCCCCGATCCTTTATCCG	70
psOo1	gene	GGCGGGGAGGCGGGGACGCAACCATGTTCCCGGCGAGCAGCTTCCACCCCTGCCCCGATCCTTTATCCG	
Oo1	gene	CAGGCCACCAAGCCGGGATGGCTGGAGGTTCGGAGCCAGGGGCTGCCGACCCGCGCCCCCTCCTTCC	140
psOo1	gene	CAGGCCACCAAGCCGGGATGGCTGGAGGTTCGGAGCCAGGGGCTGCCGACCCGCGCCCCCTCCTTCC	
Oo1	gene	TCCCCGGCTACAGACAGCTCATGGCCGCGGAGTACGTGACAGCCACCAGCGGGCACAGCTCATGGCCCT	210
psOo1	gene	TCCCCGGCTACAGACAGCTCATGGCCGCGGAGTACGTGACAGCCACCAGCGGGCACAGCTCATGGCCCT	
Oo1	gene	GCTGTGCGGATGGGTCCCCGGTCGGTCAGCAGCCGTGACGCTGCGGTGCAGGTGAACCCGCGCCGCGAC	280
psOo1	gene	GCTGTGCGGATGGGTCCCCGGTCGGTCAGCAGCCGTGACGCTGCGGTGCAGGTGAACCCGCGCCGCGAC	
Oo1	gene	GCCTCGGTGCAGTGTTCACCTCGGGCGCCGACGCTGCAGCCTGCAGGGTGCCGAGCCAGCCCCGACGCC	350
psOo1	gene	GCCTCGGTGCAGTGTTCACCTCGGGCGCCGACGCTGCAGCCTGCAGGGTGCCGAGCCAGCCCCGACGCC	
Oo1	gene	GATCGGGTTCTGTCAACCCGTTGGCCACGCGCGCGCGGAGATCCCCCGGATCCTGGCAGACCGTAGC	420
psOo1	gene	GGTCGGGTTCCTGTCAACCCGTTGGCCACGCGCGCGCGGAGATCCCCCGGATCCTGGCAGACCGTAGC	
Oo1	gene	CCCGTTCTCGTCCGTGACCTTCTGTGGCCTCTCCTCCTCACTGGAGGTTGCGGGAGGCAGGCAGACCCC	490
psOo1	gene	CCCGTTCTCGTCCGTGACCTTCTGTGGCCTCTCCTCCTCACTGGAGGTTGCGGGAGGCAGGCAGACCCC	
Oo1	gene	ACGAAGGGAGAGGGGAGCCCGGCATCCTCGGGGACCCGGAACCGGAGCCGAGAGAGGTGGCCGCGAGGA	560
psOo1	gene	ACGAAGGGAGAGGGGAGCCCGGCATCCTCGGGGACCCGGAACCGGAGCCGAGAGAGGTGGCCGCGAGGA	
Oo1	gene	AAGCGGTCCCCAGCCGCGAAGCGAGGAGGGCGATGTTTCAGGCTGCAGGGCAGGCCGGGTGGGAGCAGCA	630
psOo1	gene	AAGCGGTCCCCAGCCGCGAAGCGAGGAGGGCGACGTTTCAGGCTGCAGGGCAGGCCGGGTGGGAGCAGCA	
Oo1	gene	GCCACCACCGGAGGACCGGAACAGTGTGGCGCGGATGCAGTCTGAGCCTGGGAGCGAGGAGCCATGTCTT	700
psOo1	gene	GCCACCACCGGAGGACCGGAACAGTGTGGCGCGGATGCAGTCTGAGCCTGGGAGCGAGGAGCCATGTCTT	
Oo1	gene	GCCGAGAGATGGCTCAGGACCCCGGTGATTTCGGATGCCCTTCGAGACCAGGCCCTCCCGCAAAGCACGG	770
psOo1	gene	GCCGAGAGATGGCTCAGGACCCCGGTGATTTCGGATGCCCTTCGAGACCAGGCCCTCCCGCAAAGCACCA	
Oo1	gene	AGCAGGACAAGGAGCGCTCGTTCAGgtgaggccagcctga...intron 1 (1.8kb)... taccctgc	799
psOo1	gene	AGCAGGACAAGGAGCTCCTCGTTCAGgtgaggccagcctgg...intron 1 (1.8kb)... taccctgc	
Oo1	gene	tggtcagTTCCTTAGAGCAGAAGTACGGCTACTATCACTGCAAGGACTGCAAAATCCGGTGGGAGAGCGCT	863
psOo1	gene	tggtcagTTCCTTAGAGCAGAAGTACGGCTACTATCACTGCAAGGACTGCAAAATCCGGTGGGAGAGCGCT	
Oo1	gene	ATGTGTGGTGTGTGCAGGGCACCAGTAAGgtaagagacaccgtg...intron 2 (78bp)... tcttttctct	892
psOo1	gene	ATGTGTGGTGTGTGCAGGGCACCAGTAAGgtaagagacaccgtg...intron 2 (78bp)... tcttttctct	
Oo1	gene	cgcagGTGTACTTCAAACAGTTCGCGAGTGTGTGAGAAATCCTACAACCCCTTACAGAGTGGAGGACAT	957
psOo1	gene	cgtag GTGTACTTCAAACAGTTCGCGAGTGTGTGAGAAATCCTACAACCCCTTACAGAGTGGAGGACGT	
Oo1	gene	CACCTGTCAAgtaaaccacggtt...intron 3 (878bp)...actccgatttttcagAGTTGTAAAGAACT	982
psOo1	gene	CACCTGTCAAgtaaaccacggtt...intron 3 (878bp)...gctctgagttttcagAGTTGTAAAGAACT	

Figure 22a

Oo1 gene AGATGTGCGCTGCCCAGTCAGACTTGGCCACGTGGACCCTAAACGCCCCCATCGCAAGACTTGTGTGGA 1052
 psOo1 gene AGATGTGCGCTGCCCAGTCAGACTTGGCCACGTGTACCTTAGACGCCCCCATCGCAAGACTTGTGTGGA
 Oo1 gene GATGCAAGGACAAAAGCTTGTCTTGGACAGCACCTTCAGCTTCAAATACATCATTAGTGAGAGTACGA 1122
 psOo1 gene GATGCAAGGACAAAAGCTTGTCTTGGACAGCACCTTCAGCTTCAAATACATGATTAGTGAGAGTACGA
 Oo1 gene AACGTTTCTGCTAGATGGGGCTAATGGAATGGACAAGTGAGCTTTCTCCCTCTTCCCTCTTCCCTTTTC 1192
 psOo1 gene AACGTTTCTGCTAGATGGGGCTAATGGAATGGACAAGTGAGCTTTCTCCCTCTTCCCTCTTCCCTTTTC
 Oo1 gene CAAATTCCTCATGACAGACAGTGTACTTGGATATAAAGCCTGTGAATAAAGGTATTGCAAACA 1257
 psOo1 gene CAAATTCCTCATGACAGACAGTGTACTTGGATATAAAGCCTGTGAATAAAGGTATTGCAAACA

Figure 22b

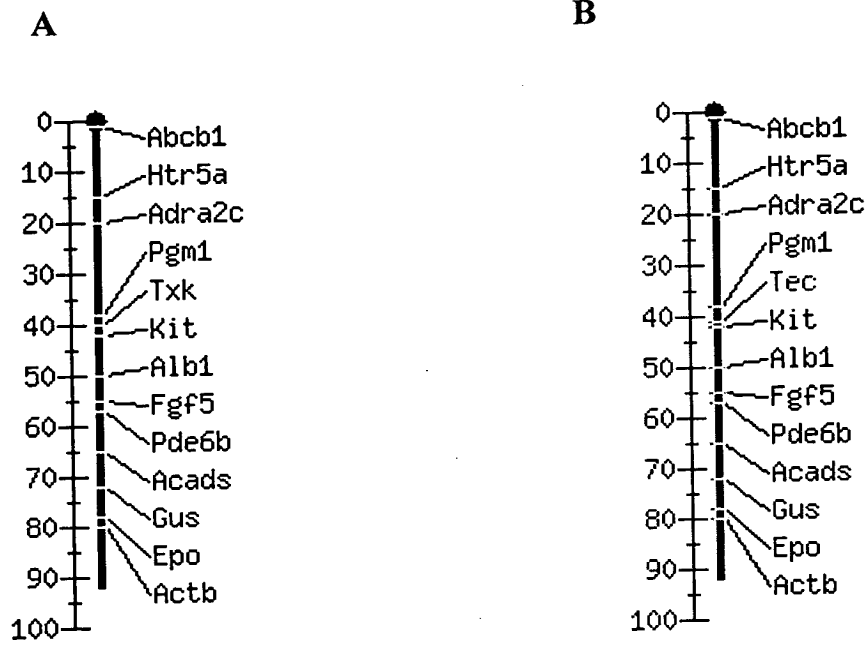


Figure 23

Oo1 Gene Targeting Strategy

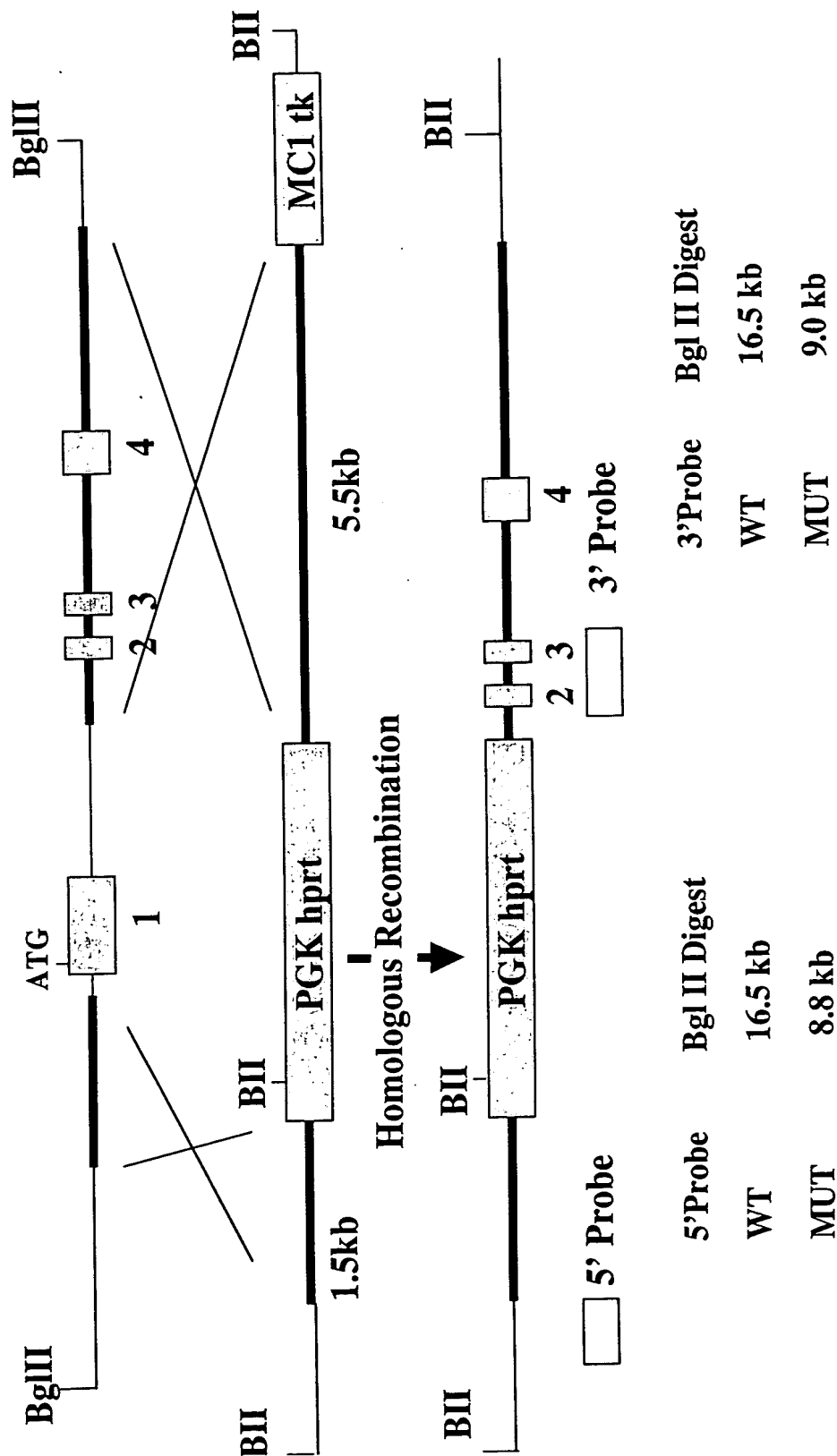


Figure 24

Human NPM2 cDNA sequence: 924bp

CAGCCCGCTT CTCTGCCCCG AGCCATGAAT CTCAGTAGCG
 CCAGTAGCAC GGAGGAAAAG GCAGTGACGA CCGTGCTCTG
 GGGCTGCGAG CTCAGTCAGG AGAGGCGGAC TTGGACCTTC
 AGACCCCAGC TGGAGGGGAA GCAGAGCTGC AGGCTGTTGC
 TTCATACGAT TTGCTTGGGG GAGAAAGCCA AAGAGGAGAT
 GCATCGCGTG GAGATCCTGC CCCCAGCAAA CCAGGAGGAC
 AAGAAGATGC AGCCGGTCAC CATTGCCTCA CTCCAGGCCT
 CAGTCCTCCC CATGGTCTCC ATGGTAGGAG TGCAGCTTTC
 TCCCCCAGTT ACTTTCAGC TCCGGGCTGG CTCAGGACCC
 GTGTTCTCA GTGGCCAGGA ACGTTATGAA GCATCAGACC
 TAACCTGGGA GGAGGAGGAG GAAGAAGAAG GGGAGGAGGA
 GGAAGAGGAA GAGGAAGATG ATGAGGATGA GGATGCAGAT
 ATATCTCTGG AGGAGCAAAG CCCTGTCAA CAAGTCAAAA
 GGCTGGTGCC CCAGAAGCAG GCGAGCGTGG CTAAGAAAAA
 AAAGCTGGAA AAAGAAGAAG AGGAAATAAG AGCCAGCGTT
 AGAGACAAGA GCCCTGTGAA AAAGGCCAAA GCCACAGCCA
 GAGCCAAGAA GCCAGGATTC AAGAAATGAG GAGCCACGCC
 TTGGGGGGCA CGGTGCAAAG TGGGCCTTCC CTGGGCTGTG
 CTGCAGGCAC AGGGTGCCCC TGTCCAGCCC CTCCACCTGT
 GTCTGAATGC AACAGGGGTG TTGCGGGGGC AACATGAGAG
 CCCCTCACCC CCAACTCTCC ACTTTCAGGA GGCCCCCAGT
 GAAGAGCCCC ACCTCGGGGT CACAATAAAG TTGCCTGGTC
 AGGAAAAAAA AAAAAAAAAA AACGTTTGCG GCCGCAAGCT
 TATG

Human NPM2 Amino Acid sequence: 214aa

MNLSSASSTE EKA VTTVLWG CELSQERRTW TFRPQLEGKQ
 SCRLLLHTIC LGEKAKEEMH RVEILPPANQ EDKKMQPVTI
 ASLQASVLPM VSMVGVQLSP PVTFLRAGS GPVFLSGQER
 YEASDLTWEE EEEEEGEEEE EEEEDDED EDADISLEEQSP
 VKQVKRLVPQ KQASVAKKKK LEKEEEEIRA SVRDKSPVKK
 AKATARAKKP GFKK

Figure 25